REMARKS

I. Status of the Claims

Claims 7, 9, 11-13, 30-32, 34 and 35 were pending in the application. Upon entry of this amendment, claims 7, 9, 11-13, 30-32, 34-37 are pending. Claims 9, 30, and 34 have been amended herein to correct typographical errors. Claims 1-6, 8, 10, 14-29, and 33 were previously cancelled. Claims 36 and 37 are newly added.

Newly added dependent claims 36 and 37 have been added to further clarify that the currently claimed methods can be practiced in combination with other known techniques for assessing a patient's risk of having cancer, such as measuring the gene expression of known cancer biomarkers. Support for this amendment is found throughout the specification and in particular, at paragraph 337 of the published version of the specification, US2005/0227917.

No new matter has been added and therefore entry of the amendments is respectfully requested.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants request reconsideration of the pending claims in view of the following remarks.

II. Priority

Applicants acknowledge that the effective filing date of the instant application is December 23, 2003 which is the filing date of Provisional Application 60/532,830.

III. Claim Objections

The typographical errors in claims 9, 30, and 34 have been corrected. Applicants request that the objection to the claims be withdrawn.

IV. Rejection under 35 U.S.C. 112, first paragraph, enablement

Claims 7, 9, 11-13, 30-32, 34, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Office alleges that the subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Applicants respectfully traverse the rejection and its supporting remarks and maintain that the specification provides more than adequate support to enable one of skill in the art to make and use the claimed invention without undue experimentation.

The Office asserts that while one of ordinary skill in the art could perform the experimentation required using standard molecular biological techniques, the amount of experimentation required to reasonably enable the claimed methods is considered undue. The Office states that the ordinary artisan would have to perform extensive amounts of trial-and-error experimentation in order to determine the following: (1) minimum increases in the expression level of SEQ ID NO: 23702 useful for reliably detecting breast cancer, colon cancer, and prostate cancer cells, (2) ethnic populations in which the expression of SEQ ID NO: 23702 can be used to reliably detect breast cancer cells, colon cancer cells, and prostate cancer cells or assess a subject's risk of having one of the aforementioned cancers, and (3) which variants of SEQ ID NO: 23702 are capable of functioning as reliable identifiers of cancerous cells or indicators of cancer.

With respect to undue experimentation, the MPEP states that, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but

whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976)."

Applicants note that the current claims do not require the detection or identification of cancer cells based solely on the expression level of SEQ ID NO: 23702, as implied in the Office's points (1)-(3) above. Rather, the currently pending claims recite that the expression of SEQ ID NO: 23702 and its variants can be used to help assess a patient's risk of having cancer wherein an increased expression of SEQ ID NO: 23702 indicates an increased risk of having cancer. In respect to the scope of the current claims, assessment indicates evaluating over-expression of SEQ ID NO: 23702 as one parameter that may be indicative, not definitive, of a cancerous phenotype. This is supported by the data in Example 105 of the specification that demonstrates a statistically significant two-fold over-expression of SEQ ID NO: 23702 in cancer tissue taken from a specific population of colon, breast, and prostate cancer patients. One of skill would no doubt take into account additional parameters when assessing and determining a patient's overall risk of having cancer.

As such, one of skill in the art would be able to use the expression data for SEQ ID NO: 23702, in combination with other diagnostic tests commonly performed in the art, to assess a patient's risk of having cancer. Thus, making and using the invention requires only routine molecular biology techniques and is a matter of routine testing of breast, colon or prostate samples for expression of SEQ ID NO: 23702 or variants thereof. While the currently pending claims encompass a large number of variants, differential expression data for these variants would be still be informative of the phenotype of the cell and would be easily measured. For claim 7 and its dependents, it would involve routine testing of cells for a gene product comprising SEQ ID NO: 23702 itself. Similarly, for claim 30 and its dependents, it would involve routine testing of tissue samples from patients for the level of nucleic acid comprising a nucleotide sequence at least 95% identical to SEQ ID NO: 23702.

The Office further alleges that the specification provides only minimal guidance and that this lack of guidance combined with the inherent unpredictability in the claimed methods would

require undue experimentation. As discussed above, the currently pending claims relate to the assessment of an increased risk of cancer by detection of over-expression of SEQ ID NO: 23702, and not detection of cancer itself. The specification provides more than adequate guidance for the presently pending claims as one of skill could easily obtain SEQ ID NO: 23702 expression data for a tissue sample suspected of being cancerous. Further, it would be routine for one of skill to incorporate this information into the evaluation of a patient's cancer phenotype. Several working examples in the specification disclose the use of differentially expressed genes as a risk assessment tool to be used in combination with other methods for evaluating a patient's cancer phenotype. Paragraph [337] embodies this practice by stating "The differential expression of these polynucleotides can be used as a diagnostic marker, a prognostic marker, for risk assessment, patient treatment and the like. These polynucleotide sequences can also be used in combination with other known molecular and/or biochemical markers." While this paragraph is specifically focused on breast cancer, the skill artisan would undoubtedly recognize that the differential gene expression of SEQ ID NO: 23702 would be a useful tool in the assessment of a patent's cancer risk.

The Offices also raises concerns regarding the statistical significance of the results stating that it is not at all clear that the results obtained for the small sample sizes tested would be considered statistically significant and that the number of patients showing a statistically significant increase in expression of SEQ ID NO: 23702 varied widely between and within the cancer types tested. Applicants assert that this variability is irrelevant. An assessment of risk of cancer does not require knowing that every single patient having cancer shows a statistically significant increase in expression of SEQ ID NO: 23702. It is sufficient to know that SEQ ID NO: 23702 is significantly over-expressed in cancerous breast, colon and prostate tissue when compared with healthy tissue in a certain percentage of patients.

In view of the above, Applicants respectfully submit that a person skilled in the art would be able to assess the increased risk of a breast, colon, or prostate cell being cancerous based on the over-expression of SEQ ID NO: 23702 using the teachings of the present application without undue experimentation. Applicants thus believe that the presently pending claims are enabled under 35 U.S.C. 112, first paragraph, and request withdrawal of the rejection.

V. Rejection under 35 U.S.C. 112, first paragraph, written description

Claims 7, 9, 11-13, 30-32, 34, and 35 are newly rejected in this Office Action under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Offices alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse the rejection and its supporting remarks. The office has not established a *prima facie* case of failure to comply with the written description requirement. The specification must be taken as complying with the first paragraph of § 112 unless there is a reason to doubt the objective truth of the statements relied upon therein for enabling support (*In re Marzocchi*, 169 USPQ 367 (CCPA 1971)). As such, the Office has not provided any reason to doubt that the specification fails to provide an adequate written description of the presently claimed invention.

The Office alleges that the specification does not contain an actual reduction to practice of the claimed methods stating that the specification does not adequately describe methods of detecting breast cancer cells, prostate cancer cells, or colon cancer cells in any ethnic population based on any level of over-expression of SEQ ID NO: 23702, and fails to adequately describe methods of assessing the risk of a human subject from any ethnic population for having breast cancer, colon cancer, or prostate cancer based on an observed increase in the expression level of SEQ ID NO: 23702 or variants having 95% or 98% identity thereto.

The central inquiry when considering written description is whether an ordinary artisan would reasonably conclude that Applicant was in possession of the claimed invention at the time of filing (see MPEP 2163 and Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1566-67,43 USPQ2d 1398, 1404-05 (Fed. Cir. 1997); Hyatt v. Boone, 146 F.3d 1348, 1354,47 USPQ2d 1128,1132 (Fed. Cir. 1998)). According to Revision I of the Written Description Training Materials, the following factors should be considered, when evaluating a claim for

compliance with the written description requirement: (a) actual reduction to practice, (b) disclosure of drawings or structural chemical formulas (c) sufficient relevant identifying characteristics (d) method of making the claimed invention, (e) level of skill and knowledge in the art, and (f) predictability in the art (see page 1 of the Training Materials).

Applicants assert that the presently pending claims do not require the detection of cancer cells based solely on the over-expression of SEQ ID NO: 23702 and that the Office is inappropriately requiring that the specification demonstrate this. The data disclosed in Example 105 clearly illustrates that over-expression of SEQ ID NO: 23702 is correlated to cancer in a certain population of colon, breast, and prostate cancer patients. Based on the information provided in the specification and the high level of skill and knowledge in the art, one of skill would recognize that a patient presenting a statistically significant, two-fold over-expression of SEQ ID NO: 23702, or variants having 95% or 98% identity thereto, has an increased risk of having a cancerous colon, breast, or prostate, irrespective of ethnic population. As such, measuring the level of SEQ ID NO: 23702 expression in a patient would be informative when assessing the patient's risk of having cancer. The specification contains clear written support for this, stating that differential gene expression data can be used in combination with other known molecular and/or biochemical markers for risk assessment. Thus, it is unquestionable that Applicants have reduced the claimed methods to practice as is evidenced by Example 105.

Even assuming that the Office has made a *prima facie* case for written description (which is traversed), the rejection is still successfully rebutted by the specification as filed in view of the state of the art at the time of filing.

The MPEP 2163(a)(1) makes clear that:

"(1) examples are not necessary to support the adequacy of a written description requirement; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known

structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). See also *Capon v. Eshhar*, 418 F.3d at 1358, 76 USPQ2d at 1084.

The Office also alleges that the specification fails to teach the relevant identifying characteristics required to satisfy the written description requirement, since it contains no discussion of the following: (1) minimum levels of over-expression of SEQ ID NO: 23702 required to reliably detect breast cancer cells, colon cancer cells, or prostate cancer cells, (2) whether the expression level of SEQ ID NO: 23702 can be used to detect cancerous cells or assess cancer risk in different ethnic populations, and (3) which variants of SEQ ID NO: 23702 are expected to be useful in detecting cancerous cells or assessing cancer risk.

The specification clearly teaches the relevant identifying characteristics of the presently claimed invention. As discussed above, the currently pending claims are directed to assessing a patient's increased risk of having cancer based on the over-expression of SEQ ID NO: 23702 and not to the detection of cancer cells based on this over-expression. The data disclosed in Example 105 clearly teach that SEQ ID NO: 23702 can be an indicative biomarker and that a statistically significant, two-fold over-expression of SEQ ID NO: 23702 is correlated with cancer in a certain population of colon, breast, and prostate cancer patients. Applicants contend that while the methods can certainly be practiced in various ethnic populations, this is irrelevant to the presently pending claims since gene expression data is evaluated on an individual patient basis against control cells obtained from the same patient.

Applicants respectfully submit that the Office has failed to provide any reasons to doubt that one of ordinary skill would recognize that Applicants had possession of the invention at the time of filing of the application and has therefore failed to make a *prima facie* case for lack of written description. Applicants therefore respectfully request that the Office withdraw the rejection of claims 7, 9, 11-13, 30-32, 34, and 35 under U.S.C. §112, first paragraph, written description.

VI. Prior Art

Applicants thank the Examiner for acknowledging that the claimed methods are free of art.

VI. Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. **03-1952** referencing docket no. **223002106600**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

In addition, please direct all further communications in this application to:

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